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(54) Intravascular stents

(57) The invention provides an intravascular stent prepared by applying to the body of a balloon-expandable stent a solution which comprises a solvent, a polymer, and a therapeutic substance and then drying the solution. Stents having a polymeric, therapeutic substance-releasing coating in which the coating is less than 0.005 cm thick and/or in which the ratio of therapeutic substance to polymer is in the range of from about 10:1 to about 1:100 form a particularly preferred aspect of the invention.

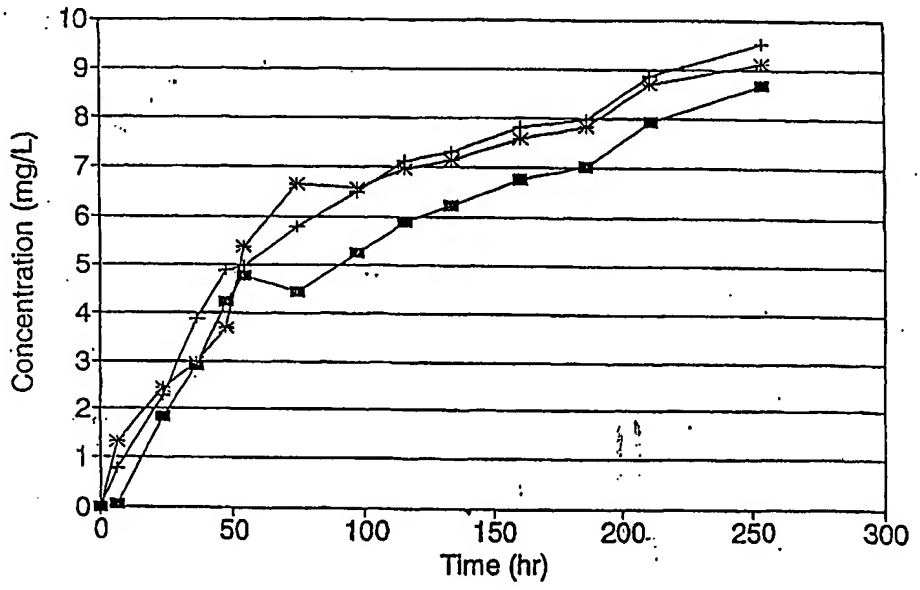

Fig. 1

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Description

[0001] This invention relates to intravascular stents for treatment of injuries to blood vessels and particularly to stents having a framework onto which a therapeutic substance or drug is applied.

[0002] Although angioplasty procedures have increased greatly in popularity for treatment of occluded arteries, the problem of restenosis following the angioplasty treatment remains a significant problem. Restenosis is the closure of a peripheral or coronary artery following trauma to the artery caused by efforts to open an occluded portion of the artery by angioplasty, such as, for example, by balloon dilation, atherectomy or laser ablation treatment of the artery. For these angioplasty procedures, restenosis occurs at a rate of about 30-60% depending upon the vessel location, lesion length and a number of other variables.

[0003] One aspect of restenosis may be simply mechanical; e.g. caused by the elastic rebound of the arterial wall and/or by dissections in the vessel wall caused by the angioplasty procedure. These mechanical problems have been successfully addressed by the use of stents to tack-up dissections and prevent elastic rebound of the vessel, thereby reducing the level of restenosis for many patients. The stent is typically inserted by catheter into a vascular lumen and expanded into contact with the diseased portion of the arterial wall, thereby providing internal support for the lumen. Examples of stents which have been successfully applied over a PTCA balloon and radially expanded at the same time as the balloon expansion of an affected artery include the stents disclosed in US-A-4733665 (Palmaz), US-A-4800882 (Gianturco) and US-A-4886062 (Wiktor) which are incorporated herein by reference in their entirety.

[0004] Another aspect of restenosis is believed to be a natural healing reaction to the injury of the arterial wall that is caused by angioplasty procedures. The final result of the complex steps of the healing process is intimal hyperplasia, the migration and proliferation of medial smooth muscle cells, until the artery is again occluded.

[0005] To address both aspects of the restenosis problem, it has been proposed to provide stents which are seeded with endothelial cells (see Dichek,D.A. et al. "Seeding of Intravasoular Stents With Genetically Engineered Endothelial Cells", Circulation 80: 1347-1353 (1989)). In that experiment, sheep endothelial cells that had undergone retrovirus-mediated gene transfer for either bacterial beta-galactosidase or human tissue-type plasminogen activator were seeded onto stainless steel stents and grown until the stents were covered. The cells were therefore able to be delivered to the vascular wall where they could provide therapeutic proteins. Other methods of providing therapeutic substances to the vascular wall include simple heparin-coated metallic stents, whereby a heparin coating is ionically or covalently bonded to the stent. Still other methods of providing therapeutic substances to the vascular wall by means of stents have also been proposed such as in US-A-5102417 (Palmaz), WO-91/12779 "Intraluminal Drug Eluting Prosthesis" and WO-90/13332 "Stent With Sustained Drug Delivery". In the latter two, it is suggested that antiplatelet agents, anticoagulant agents, antimicrobial agents, antimetabolic agents and other drugs could be supplied in stents to reduce the incidence of restenosis.

[0006] Metal stents such as those disclosed in US-A-4733665 (Palmaz), US-A-4800882 (Gianturco) and US-A-4886062 (Wiktor) could be suitable for drug delivery in that they are capable of maintaining intimate contact between a substance applied to the outer surface of the stent and the tissues of the vessel to be treated. However, there are significant problems to be overcome in order to secure a therapeutically significant amount of a substance onto the metal of the stent; to keep it on the stent during expansion of the stent into contact with the blood vessel wall; and also controlling the rate of drug delivery from the drug on the stent to the vessel wall.

[0007] There thus remains a need for means for providing a stent having a therapeutically significant amount of a drug applied thereto.

[0008] We have discovered a method for making an intravascular stent which meets this need.

[0009] Viewed from one aspect therefore the invention provides a method for making an intravascular stent comprising the steps of:

(a) providing a generally cylindrical stent body;
(b) applying to the stent body a solution which comprises a solvent, a polymer dissolved in the solvent and a therapeutic substance dispersed in the solvent; and
(c) evaporating said solvent.

[0010] Viewed from a further aspect the invention provides the use of a solution containing a dissolved polymer and a dispersed therapeutic substance for the manufacture of a therapeutic agent comprising an intravascular stent having a polymeric drug-eluting surface coating.

[0011] Viewed from a still further aspect the invention provides stents made by the method of the invention.

[0012] In the method of the invention there is applied to the body of a stent, and in particular to its tissue-contacting surface, a solution which includes a solvent, a polymer dissolved in the solvent and a therapeutic substance (i.e. a drug) dispersed in the solvent, and the solvent thereafter is evaporated to leave a drug-elating polymeric surface on the stent. The inclusion of a polymer in intimate contact with a drug on the stent allows the drug to be retained on the

stent in a resilient matrix during expansion of the stent and also slows the administration of drug following implantation. The method of the invention can be used whether the stent has a metallic or polymeric surface. The method is also an extremely simple one since it can be effected by simply immersing the stent into the solution or by spraying the solution onto the stent. The amount of drug to be included on the stent can be readily controlled by applying multiple thin coats of the solution while allowing it to dry between coats. The overall coating should be generally thin enough so that it will not significantly increase the profile of the stent for intravascular delivery by catheter. It is therefore preferably less than about 0.002 inch (0.05 mm) thick and most preferably less than 0.001 inch (0.025 mm) thick. The adhesion of the coating and the rate at which the drug is delivered can be controlled by the selection of an appropriate bioabsorbable or biostable polymer and by the ratio of drug to polymer in the solution. By this method, drugs such as glucocorticoids (e.g. dexamethasone, betamethasone), heparin, hirudin, tocopherol, angiopeptin, aspirin, ACE inhibitors, growth factors, oligonucleotides, and, more generally, antiplatelet agents, anticoagulant agents, antimitotic agents, antioxidants, antimetabolite agents, and anti-inflammatory agents can be applied to a stent, retained on a stent during expansion of the stent and elute the drug at a controlled rate. The release rate can be further controlled by varying the ratio of drug to polymer in the multiple layers. For example, a higher drug-to-polymer ratio in the outer layers than in the inner layers would result in a higher early dose which would decrease over time.

[0013] In operation, the stent made according to the present invention can deliver drugs to a body lumen by introducing the stent transluminally into a selected portion of the body lumen and radially expanding the stent into contact with the body lumen. The transluminal delivery can be accomplished by a catheter designed for the delivery of stents and the radial expansion can be accomplished by balloon expansion of the stent, by self-expansion of the stent, or a combination of self-expansion and balloon expansion.

[0014] Thus the present invention provides a stent which may be delivered and expanded in a selected blood vessel without losing a therapeutically significant amount of a drug applied thereto. It also provides a drug-containing stent which allows for a sustained release of the drug to vascular tissue.

[0015] The underlying structure of the stent used according to the invention can be virtually any stent design, for example of the self-expanding type or of the balloon-expandable type, and of metal or polymeric material. Thus metal stent designs such as those disclosed in US-A-4733665 (Palmaz), US-A-4800882 (Gianturco) and US-A-4886062 (Wiktor) could be used in the present invention. The stent could be made of virtually any bio-compatible material having physical properties suitable for the design. For example, tantalum and stainless steel have been proven suitable for many such designs and could be used in the present invention. Also, stents made with biostable or bioabsorbable polymers such as poly(ethylene terephthalate), polyacetal, poly(lactic acid), poly(ethylene oxide)/poly(butylene terephthalate) copolymer could be used in the present invention. Although the stent surface should be clean and free from contaminants that may be introduced during manufacturing, the stent surface requires no particular surface treatment in order to retain the coating applied in the present invention. Both the inner and outer surfaces of the stent may be provided with the coating according to the present invention.

[0016] In order to provide the coated stent according to the present invention, a solution which includes a solvent, a polymer dissolved in the solvent and a therapeutic substance dispersed in the solvent is first prepared. The solvent, polymer and therapeutic substance should of course be mutually compatible. The solvent should be capable of placing the polymer into solution at the concentration desired. Moreover the solvent and polymer should not chemically alter the therapeutic character of the therapeutic substance. However, the therapeutic substance only needs to be dispersed throughout the solvent so that it may be either in a true solution with the solvent or dispersed in fine particles in the solvent. Examples of some suitable combinations of polymer, solvent and therapeutic substance are set forth in Table 1 below.

TABLE 1

POLYMER	SOLVENT	THERAPEUTIC SUBSTANCE
poly(L-lactic acid)	chloroform	dexamethasone
poly(lactic acid-co-glycolic acid)	acetone	dexamethasone
polyether urethane	N-methyl pyrrolidone	tocopherol (vitamin E)
silicone adhesive	xylene	dexamethasone phosphate
poly(hydroxy-butyrate-co-hydroxyvalerate)	dichloro-methane	aspirin
fibrin	water (buffered saline)	heparin

[0017] The solution is applied to the stent and the solvent is allowed to evaporate, thereby leaving on the stent surface a coating of the polymer and the therapeutic substance. Typically, the solution can be applied to the stent by either spraying the solution onto the stent or immersing the stent in the solution. Whether one chooses application by immersion or application by spraying depends principally on the viscosity and surface tension of the solution, however, it has

been found that spraying in a fine spray such as that available from an airbrush will provide a coating with the greatest uniformity and will provide the greatest control over the amount of coating material to be applied to the stent. In either a coating applied by spraying or by immersion, multiple application steps are generally desirable to provide improved coating uniformity and improved control over the amount of therapeutic substance to be applied to the stent.

[0018] The polymer chosen should be a polymer that is biocompatible and minimizes irritation to the vessel wall when the stent is implanted. The polymer may be either a biostable or a bioabsorbable polymer depending on the desired rate of release or the desired degree of polymer stability, but a bioabsorbable polymer may be more desirable since, unlike a biostable polymer, it will not be present long after implantation to cause any adverse, chronic local response. Bioabsorbable polymers that could be used include poly(L-lactic acid), polycaprolactone, poly(lactide-co-glycolide), poly(hydroxybutyrate), poly(hydroxybutyrate-co-valerate), polydioxanone, polyorthoester, polyanhydride, poly(glycolic acid), poly(D,L-lactic acid), poly(glycolic acid-co-trimethylene carbonate), polyphosphoester, polyphosphoester urethane, poly(amino acids), cyanoacrylates, poly(trimethylene carbonate), poly(iminocarbonate), copoly (ether-esters) (e.g. PEO/PLA), polyalkylene oxalates, polyphosphazenes and biomolecules such as fibrin, fibrinogen, cellulose, starch, collagen and hyaluronic acid. Also, biostable polymers with a relatively low chronic tissue response such as polyurethanes, silicones, and polyesters could be used and other polymers could also be used if they can be dissolved and cured or polymerized on the stent such as polyolefins, polyisobutylene and ethylene-alphaolefin copolymers; acrylic polymers and copolymers, vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride and polyvinylidene chloride; polyacrylonitrile, polyvinyl ketones; polyvinyl aromatics, such as polystyrene, polyvinyl esters, such as polyvinyl acetate; copolymers of vinyl monomers with each other and olefins, such as ethylene-methyl methacrylate copolymers, acrylonitrile-styrene copolymers, ABS resins, and ethylene-vinyl acetate copolymers; polyamides, such as Nylon 66 and polycaprolactam; alkyd resins; polycarbonates; polyoxymethylenes; polyimides; polyethers; epoxy resins, polyurethanes; rayon; rayon-triacetate; cellulose, cellulose acetate, cellulose butyrate; cellulose acetate butyrate; cellophane; cellulose nitrate; cellulose propionate; cellulose ethers; and carboxymethyl cellulose.

[0019] The ratio of therapeutic substance to polymer in the solution will depend on the efficacy of the polymer in securing the therapeutic substance onto the stent and the rate at which the coating is to release the therapeutic substance to the tissue of the blood vessel. More polymer may be needed if it has relatively poor efficacy in retaining the therapeutic substance on the stent and more polymer may be needed in order to provide an elution matrix that limits the elution of a very soluble therapeutic substance. A wide ratio of therapeutic substance to polymer could therefore be appropriate and the weight ratio could range from about 10:1 to about 1:100.

[0020] The therapeutic substance used in the present invention could be virtually any therapeutic substance which possesses desirable therapeutic characteristics for application to a blood vessel. This can include both solid substances and liquid substances. For example, glucocorticoids (e.g. dexamethasone, betamethasone), heparin, hirudin, tocopherol, angiopeptin, aspirin, ACE inhibitors, growth factors, oligonucleotides, and, more generally, antiplatelet agents, anticoagulant agents, antimitotic agents, antioxidants, antimetabolite agents, and anti-inflammatory agents could be used. Antiplatelet agents can include drugs such as aspirin and dipyridamole. Aspirin is classified as an analgesic, antipyretic, anti-inflammatory and antiplatelet drug. Dipyridimole is a drug similar to aspirin in that it has anti-platelet characteristics. Dipyridimole is also classified as a coronary vasodilator. Anticoagulant agents can include drugs such as heparin, coumadin, protamine, hirudin and tick anticoagulant protein. Antimitotic agents and antimetabolite agents can include drugs such as methotrexate, azathioprine, vincristine, vinblastine, fluorouracil, adriamycin and mutamycin.

[0021] Embodiments of the invention will now be described further with reference to the following non-limiting Examples and the accompanying drawings, in which:

Fig. 1 is a plot showing elution profiles for stents according to the present invention with a coating of dexamethasone and poly(L-lactic acid) made according to Example 6; and

Fig. 2 is a plot showing elution profiles for sterilized stents according to the present invention with a coating of dexamethasone and poly(L-lactic acid) made according to Example 7.

[0022] In the Examples percentages and ratios are by weight unless otherwise stated.

EXAMPLE 1 (COMPARATIVE)

[0023] A 1% solution of dexamethasone in acetone was made, forming a clear solution. The solution was placed in an airbrush reservoir (Badger #200). Wiktor type tantalum wire stents were sprayed with the solution in short bursts while rotating the stents. The acetone quickly evaporated from the stents, leaving a white residue on the stent wire. The process was continued until all of the stent wires were coated. The drug elution rate for the stent was determined by immersing the stent in phosphate buffered saline solution (pH=7.4). Traces of dexamethasone were observed to remain on the immersed stents for less than 31 hours.

EXAMPLE 2 (COMPARATIVE)

[0024] A 2% solution of dexamethasone in acetone was made, forming a solution with suspended particles of dexamethasone. The solution was placed into a tube. Wiktor type tantalum wire stents were dipped rapidly and were allowed to dry. Each stent was dipped into the solution 12-15 times to provide a white surface coating. Two stents were placed on an angioplasty balloon and were inflated on the balloon. Approximately 80% of the dexamethasone coating flaked off of the stents.

EXAMPLE 3

[0025] A solution of 1% dexamethasone and 0.5% poly(caprolactone) (Aldrich 18,160-9) in acetone was made. The solution was placed into a tube. Wiktor type tantalum wire stents were dipped rapidly and were allowed to dry. Each stent was dipped into the solution 12-15 times to provide a white surface coating. A stent so coated was expanded on a 3.5mm angioplasty balloon causing a significant amount of the coating to become detached.

EXAMPLE 4

[0026] A solution of 1% dexamethasone and 0.5% poly(L-lactic acid) (Medisorb) in acetone was made. The solution was placed into a tube. Wiktor type tantalum wire stents were dipped rapidly and were allowed to dry. Each stent was dipped into the solution 12-15 times to provide a white surface coating. A stent so coated was expanded on a 3.5mm angioplasty balloon causing only a small portion of the coating (less than 25%) to become detached)

EXAMPLE 5

[0027] A solution including a 2% dispersion of dexamethasone and a 1% solution of poly(L-lactic acid) (CCA Biochem MW=550,000) in chloroform was made. The solution was placed into an airbrush (Badger). Wiktor type tantalum wire stents were sprayed in short bursts and were allowed to dry. Each stent was sprayed with the solution about 20 times to provide a white surface coating. A stent so coated was expanded on a 3.5mm angioplasty balloon. The coating remained attached to the stent throughout the procedure.

EXAMPLE 6

[0028] A solution including a 2% dispersion of dexamethasone and a 1% solution of poly(L-lactic acid) (CCA Biochem MW=550,000) in chloroform was made. The solution was placed into an airbrush (Badger #250-2). Wiktor type tantalum wire stents were suspended from a fixture and sprayed in 24 short bursts (6 bursts from each of the four directions perpendicular to the stent axis) and were allowed to dry. The resulting stents had a coating weight of about 0.0006-0.0015 grams. Three of the stents were tested for long term elution by placing one stent in 3.0 ml of phosphate buffered saline solution (pH=7.4) at ambient temperature without stirring. The amount of dexamethasone eluted was evaluated by measuring absorbance at 244 nm in a UV-VIS spectrophotometer. The results of this test are shown in Figure 1.

EXAMPLE 7

[0029] A solution including a 2% dispersion of dexamethasone and a 1% solution of poly(L-lactic acid) (Medisorb 100-L) in chloroform was made along with a control solution of 1% of poly(L-lactic acid) (Medisorb 100-L) in chloroform. The solutions were placed into an airbrush (Badger #250-2). Wiktor type tantalum wire stents were expanded on a 3.0mm balloon, suspended from a fixture and sprayed in 16 short bursts (2-3 bursts of about 1 second followed by several minutes drying time between applications). The resulting dexamethasone-coated stents had an average coating weight of about 0.0012 grams while the polymer-coated stents had an average polymer weight of about 0.0004 grams. The stents were sterilized in ethylene oxide. Three of the sterilized dexamethasone-coated stents were tested for long term elution by placing one stent in 3.0 ml of phosphate buffered saline solution (pH=7.4) at ambient temperature without stirring. The amount of dexamethasone eluted was evaluated by measuring absorbance at 244 nm in a UV-VIS spectrophotometer. The results of this test are shown in Figure 2. Dexamethasone-coated stents and polymer-coated control stents were implanted in the coronary arteries of 8 pigs (N=12 for each type) according to the method set forth in "Restenosis After Balloon Angioplasty - A Practical Proliferative Model in Porcine Coronary Arteries," by Robert S. Schwartz et al., Circulation 82(6):2190-2200 (1990), and "Restenosis and the Proportional Neointimal Response to Coronary Artery Injury: Results in a Porcine Model" by Robert S. Schwartz et al., J Am Coll Cardiol 19:267-274 (1992) with the result that when compared with the controls, the dexamethasone-coated stents reduced the amount of prolif-

eration associated with the arterial injury.

Claims

1. An intravascular stent comprising a generally cylindrical stent body having a polymeric drug-eluting surface coating wherein the stent is obtainable by a method comprising the steps of:

   (a) providing a generally cylindrical balloon-expandable stent body;
   (b) applying to the stent body a solution which comprises a solvent, a polymer, and a therapeutic substance; and
   (c) drying said solution whereby to provide a coating to the stent body of a polymer and the therapeutic substance.

2. An intravascular stent as claimed in claim 1 comprising a generally cylindrical stent body having a polymeric drug-eluting surface coating wherein the stent is obtainable by a method comprising the steps of:

   (a) providing a generally cylindrical balloon-expandable stent body;
   (b) applying to the stent body a solution which comprises a solvent, a polymer, and a therapeutic substance; and
   (c) drying said solution whereby to provide a coating to the stent body of a polymer and the therapeutic substance in which the coating is less than 0.005 cm thick.

3. An intravascular stent as claimed in claim 1 comprising a generally cylindrical stent body having a polymeric drug-eluting surface coating wherein the stent is obtainable by a method comprising the steps of:

   (a) providing a generally cylindrical balloon-expandable stent body;
   (b) applying to the stent body a solution which comprises a solvent, a polymer, and a therapeutic substance wherein the ratio of therapeutic substance to polymer is in the range of from about 10:1 to about 1:100; and
   (c) drying said solution whereby to provide a coating to the stent body of a polymer and the therapeutic substance.

4. A stent obtainable by a method as defined in any one of claims 1 to 3 further comprising the step of repeating the step of applying to the stent body a solution which comprises a solvent, a polymer, and a therapeutic substance.

5. A stent obtainable by a method as defined in any one of claims 1 to 3 wherein the solution comprises a solvent, a polymer dissolved in the solvent and a therapeutic substance dissolved in the solvent.

6. A stent obtainable by a method as defined in claim 5 further comprising the step of repeating the step of applying to the stent body the solution comprising a solvent, a polymer dissolved in the solvent and a therapeutic substance dissolved in the solvent.

7. A stent obtainable by a method as defined in any one of claims 1 to 3 wherein the solution comprises a solvent, a polymer dissolved in the solvent and a therapeutic substance dispersed in the solvent.

8. A stent obtainable by a method as defined in claim 7 further comprising the step of repeating the step of applying to the stent body the solution comprising a solvent, a polymer dissolved in the solvent and a therapeutic substance dispersed in the solvent.

9. A stent obtainable by a method as defined in any one of claims 1 to 8 wherein said stent body has a metal surface.

10. A stent obtainable by a method as defined in any one of claims 1 to 8 wherein said stent body has a polymeric surface.

11. A stent obtainable by a method as defined in any one of claims 1 to 10 wherein said solution is applied to said body by spraying.

12. A stent obtainable by a method as defined in any one of claims 1 to 10 wherein said solution is applied to said body by immersion.

13. A stent obtainable by a method as defined in any one of claims 1 to 12 wherein said solution is applied to said body in a plurality of application and drying steps.

14. A stent obtainable by a method as defined in claim 13 wherein the concentration ratio of said therapeutic substance to said polymer in said solution is varied between some of said plurality of application steps.

15. A stent obtainable by a method as defined in any one of claims 1 to 14 wherein said polymer is a bioabsorbable polymer.

16. A stent obtainable by a method as defined in claim 15 wherein said polymer is selected from poly(L-lactic acid), poly(lactide-co-glycolide) and poly(hydroxybutyrate-co-valerate).

17. A stent obtainable by a method as defined in any one of claims 1 to 14 wherein said polymer is a biostable polymer.

18. A stent obtainable by a method as defined in claim 17 wherein said polymer is selected from silicones, polyurethanes, polyesters, vinyl homopolymers and copolymers, acrylate homopolymers and copolymers, polyethers and cellulosics.

19. A stent obtainable by a method as defined in any one of claims 1 to 14 wherein said polymer is selected from poly (L-lactic acid), poly(lactide-co-glycolide), fibrin, silicone, polyurethane, and poly(phosphoester urethane).

20. A stent obtainable by a method as defined in any one of claims 1, 2 and 4 to 19 wherein the weight ratio of said therapeutic substance to said polymer in said solution is in the range of about 10:1 to 1:100.

21. A stent obtainable by a method as defined in any one of claims 1 to 20 wherein said therapeutic substance is selected from glucocorticoids, dexamethasone, dexamethasone sodium phosphate, anticoagulants, heparin, hirudin, tick anticoagulant peptide, angiopeptin, antimitotic agents, and oligonucleotides.

22. A stent obtainable by a method as defined in claim 21 wherein said therapeutic substance is an antimitotic agent.

23. A stent obtainable by a method as defined in any preceding claim wherein step (c) comprises evaporating said solvent.

24. A method for making an intravascular stent comprising the steps of:

(a) providing a generally cylindrical balloon-expandable stent body;
(b) applying to the stent body a solution which comprises a solvent, a polymer, and a therapeutic substance; and
(c) drying said solution whereby to provide a coating to the stent body of a polymer and the therapeutic substance.

25. A method for making an intravascular stent comprising the steps of:

(a) providing a generally cylindrical balloon-expandable stent body;
(b) applying to the stent body a solution which comprises a solvent, a polymer, and a therapeutic substance; and
(c) drying said solution whereby to provide a coating to the stent body of a polymer and the therapeutic substance in which the coating is less than 0.005 cm thick.

26. A method for making an intravascular stent comprising the steps of:

(a) providing a generally cylindrical balloon-expandable stent body;
(b) applying to the stent body a solution which comprises a solvent, a polymer, and a therapeutic substance wherein the ratio of therapeutic substance to polymer is in the range of from about 10:1 to about 1:100; and
(c) drying said solution whereby to provide a coating to the stent body of a polymer and the therapeutic substance.

27. A balloon-expandable stent having a polymeric, therapeutic substance-releasing coating in which the coating is less than 0.005 cm thick.

28. A balloon-expandable stent having a polymeric, therapeutic substance-releasing coating in which the ratio of therapeutic substance to polymer in said coating is in the range of from about 10:1 to about 1:100.

29. A stent as claimed in claim 27 or claim 28 wherein said coating comprises a therapeutic substance which is an antimitotic agent or an oligonucleotide.

30. A stent as claimed in any one of claims 27 to 29 wherein said coating comprises a polymer which is bioabsorbable or biostable.

31. A stent as claimed in claim 30 wherein said polymer is selected from poly(L-lactic acid), poly(lactide-co-glycolide), poly(hydroxybutyrate-co-valerate), silicones, polyurethanes, polyesters, vinyl homopolymers and copolymers, acrylate homopolymers and copolymers, polyethers and cellulosics.

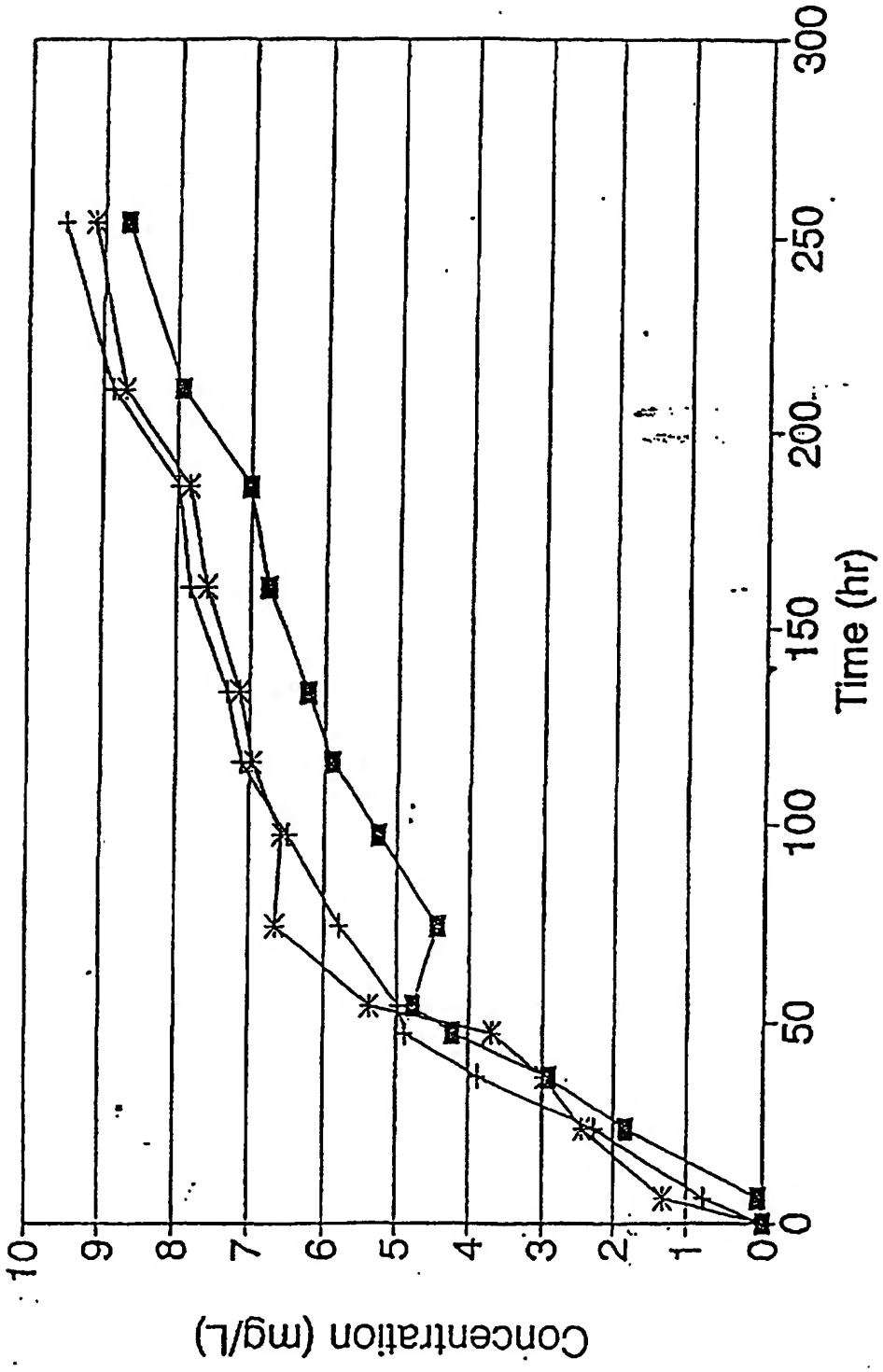
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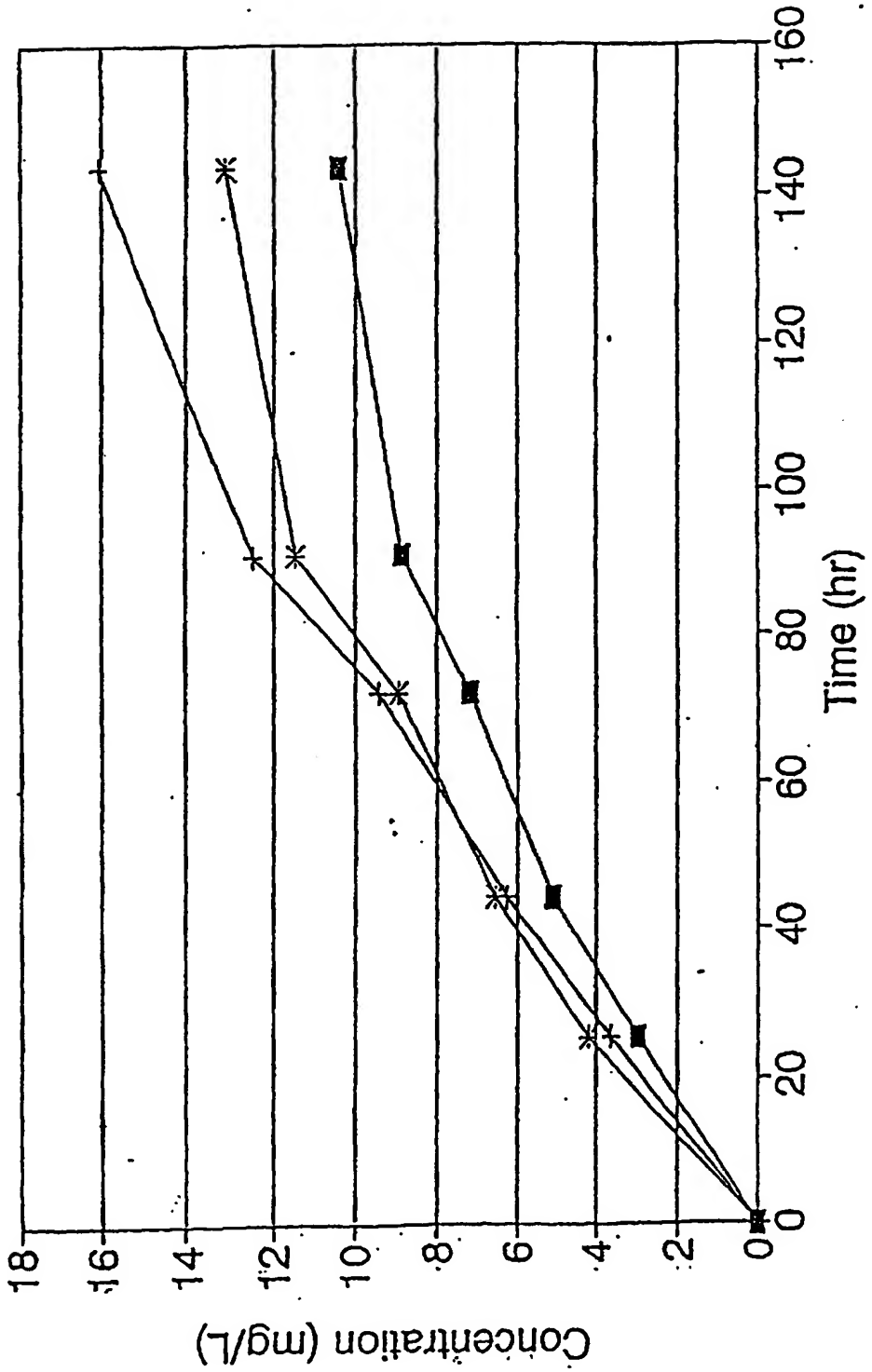
Fig. 1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140
160
Time (hr)

Fig. 2

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 01 12 6059

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	WO 92 15286 A (NOVA PHARMACEUTICAL CORP.) 17 September 1992 (1992-09-17) * page 9, line 6 - line 17 * * page 10; example 7 *	1-31	A61L31/00 A61F2/06
X	WO 91 18940 A (NOVA PHARMACEUTICAL CORP.) 12 December 1991 (1991-12-12) * page 6, line 1 * * page 10, line 18 - line 20 * * page 11, line 1 - line 5 * * page 27, line 20 - line 23; claims *	1-15	
X	WO 93 06792 A (SCIMED LIFE SYSTEMS, INC.) 15 April 1993 (1993-04-15) * page 21, line 18 - line 31; claims *	1	
A	WO 91 17789 A (STACK, RICHARD,S. ET AL.) 28 November 1991 (1991-11-28) * page 21, line 18 - line 37 * * page 22, line 1 - line 3 * * page 27, line 11 - line 14 *	1-31	
D,A	WO 91 12779 A (MEDTRONIC, INC.) 5 September 1991 (1991-09-05) * page 3, line 4 - line 14 * * page 10, line 32 - line 38 * * page 12, line 23 - line 28 * * page 13, line 5 - line 6 * * page 13, line 16 - line 17 *	1	TECHNICAL FIELDS SEARCHED (Int.Cl.7) A61L A61F
P,X	EP 0 566 245 A (MEDTRONIC, INC.) 20 October 1993 (1993-10-20) * column 6, line 2 - line 17 * * column 8, line 19 - line 21 *	1	

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	14 December 2001	ESPINOSA, M

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
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